**Amendments to the Specification**

Please delete the section entitled "Brief Description of the Figures," i.e., delete the text beginning at page 10, line 1, through page 13, line 6.

Please replace the paragraph beginning at page 17, line 14, with the following amended paragraph:

Copolymer 1 and D-Copolymer 1 were shown to prevent GVHD in a murine model of lethal GVHD which mimics matched bone marrow transplantation in humans (see U.S. Patent No. 5,858,964, and particularly Figures 4 and 5 thereof, and Figure 3 of Schlegel et al., 1996) ~~and Figs. 3-5 herein in the present application~~). According to the present invention, random copolymers other than Copolymer 1 and D-Copolymer 1 are envisaged for use in the prevention and treatment of GVHD.

Please replace the paragraph beginning at page 17, line 21, with the following amended paragraph:

According to the present invention, Copolymer 1, D-Copolymer 1 and other random copolymers are envisaged to prevent or significantly delay graft rejection. As shown in the Examples hereinafter, Copolymer 1 is effective in suppressing in mice the rejection of grafts received from another mouse strain of the same MHC haplotype. Thus, graft rejection could be suppressed in BALB/c mice receiving grafts from B10.D2 donor mice, in C3HSH mice receiving grafts from

C57BL donor mice, and in PJL mice receiving grafts from B10PL donor mice (see ~~Figs. 6-8 and~~ Tables 4 and 5 herein). These transplantation mouse models are similar to the MHC matched organ transplantation in humans. Moreover, Copolymer 1 is also effective in suppressing in mice rejection of grafts from strains of different MHC haplotypes, for example, suppressing in BALB/c mice rejection of grafts received from C57BL donor mice (see Tables 4 and 5 herein), a model which is similar to the MHC unmatched organ transplantation in humans. Thus, pre- and post-transplantation administration of Copolymer 1 over a limited time after transplantation can significantly reduce the incidence, onset and severity of immunorejection, resulting in improved long-term survival.

Please replace the paragraph beginning at page 26, line 33, with the following amended paragraph:

As shown in Fig. 1A of U.S. patent no. 5,858,964 for stimulator cells of PL/J mice and in Fig. 1B of that patent for stimulator cells of BALB/c mice, Copolymer 1 (Batch I; 20 μg/well) significantly inhibited MLR across minor as well as major histocompatibility barriers. 63% and 77% inhibition could be obtained, respectively, when 1:1 ratio of responder to stimulator cells was used, while the MBP 89-101 and the KM-core peptides (at the same concentration, i.e. 20 μg/well), which are specific to the H-$2^s$ haplotype, did not induce any

significant effect. The inhibition obtained by Copolymer 1 was similar (in response to minor histocompatibility antigen) or even higher (in response to major histocompatibility antigen) than the inhibition obtained with the combination of the two synthetic peptides Ac 1-11[4A] and MBP 35-47, which specifically bind to the class II molecules I-$A^u$ and the I-$E^u$, respectively. The molar efficiency of Copolymer 1 of M.W. 6000 is even higher since the molecular weight of the synthetic peptides is 4-5 fold lower.

Please replace the paragraph beginning at page 27, line 18, with the following amended paragraph:

The effect of Copolymer 1 (Batch I) on mixed lymphocyte cultures across major histocompatibility barriers was tested. T cell proliferation was assessed in six different MHC-disparate strain combinations. Data given in Figs. ~~2A-E~~1A-1E of Schlegel et al. (1996) are representative of five separate experiments with similar results. In all experiments, addition of Copolymer 1 (10-100 µg/well) resulted in a dose-dependent inhibition of the MLC. HEL showed no or only minimal inhibitory effect at all concentrations tested (Figs. ~~2A-E~~1A-1E of Schlegel et al., 1996). 10-25 µg/well of Copolymer 1 was sufficient to achieve 50% inhibition of the proliferative responses. Maximum inhibition (100%) was obtained in all strain combinations tested. To exclude the

possibility that higher concentrations of Copolymer 1 (50-100 μg/well) might be toxic to the responder cells, responder cells from background wells and from wells incubated with 25-100 μg/well of Copolymer 1 in the presence of stimulator cells for 72 hours in a primary assay, were rechallenged in a subsequent secondary assay with IL-2 (5,000 U/well). As shown in Table 1, there was no difference between the secondary proliferative responses of the groups tested. Responder cells that had been incubated with stimulator cells in the presence of Copolymer 1 for 72 hours were equally responsive to IL-2 compared to non-treated cells.

Please replace the paragraph beginning at page 32, line 12, with the following amended paragraph:

(ii) Effect of Copolymer 1 Treatment on the Incidence, Onset and Severity of GVHD. Recipient mice were pretreated with 600 μg of Copolymer 1 (Batch I) or with the respective controls (PBS, HEL) on day -1. For the first five weeks after transplant mice were injected daily as outlined in Materials and Methods, followed by a tapering schedule over an additional four weeks. Data from three consecutive experiments are summarized in Figures 3A-D of Schlegel et al. (1996). Administration of Copolymer 1 significantly reduced the overall incidence of GVHD (as determined by typical skin changes and weight loss) from 100% (26/26, 10/10) in control

mice to 12% (3/25) ($P < 0.001$) in Copolymer 1-treated animals on day 30 after transplant and from 100% in controls to 12/25 (48%) on day 70 after transplant ($P > 0.02$). Figure 3A of Schlegel et al. (1996) depicts the onset of GVHD in individual mice of the different experimental groups. In 12/25 animals treated with Copolymer 1 the onset of GVDH was delayed with a range of 32-112 days after transplant (median of 73 days) as compared to control mice treated with either PBS (median onset of 21 days) or HEL (median onset 22 days). Nine of 25 animals treated with the observation period of 140 days after transplant (Fig. 3A of Schlegel et al., 1996). Furthermore, treatment with Copolymer 1 improved overall disease severity as gauged by the disease severity score (Fig. 3B of Schlegel et al., 1996) and by mean body weight curves of transplanted animals (Fig. 3D of Schlegel et al., 1996).

Please replace the paragraph beginning at page 33, line 3, with the following amended paragraph:

(iii) Effect of Copolymer 1 treatment on survival. Treatment with Copolymer 1 (Batch I) improved long-term survival from lethal graft-versus-host disease. As shown in Fig. 3C of Schlegel et al. (1996), 14/25 (56%) of Copolymer 1-treated mice survived more than 140 days after transplant as compared to 2/26 of PBS treated or to 1/10 of HEL treated

control mice ($P < 0.01$). Treatment with HEL did not improve long-term survival.

Please replace the paragraph beginning at page 33, line 11, with the following amended paragraph:

Similar experiments were performed using Copolymer 1 Batch I (Fig. ~~4A~~2A of U.S. patent no. 5,858,964) or Batch II (Fig. ~~4B~~2B of U.S. patent no. 5,858,964). Thus, treatment with Copolymer 1 for the first nine weeks after bone marrow transplantation improved long-term survival from lethal GVHD.

Please replace the paragraph beginning at page 34, line 7, with the following amended paragraph:

The results are shown in Fig. ~~5~~3 of U.S. patent no. 5,858,964 and Table 3. D-Copolymer 1 treatment reduced the overall incidence of GVHD after allogeneic bone marrow transplantation from 100% (7/7) in control mice to 43% (3/7) in D-Copolymer 1-treated animals on day 30. Two of seven animals treated with D-Copolymer 1 did not develop any signs of GVHD beyond the observation period of 140 days after transplantation. Furthermore, treatment with D-Copolymer 1 improved overall disease severity as gauged by the mean disease score (Table 3).

Please replace the paragraph beginning at page 36, line 1, with the following amended paragraph:

(ii) Effect of D-Copolymer 1 Treatment on Survival. Treatment with D-Copolymer 1 improved long-term survival from lethal graft-versus-host disease. As shown in Fig. ~~5~~ 3 of U.S. patent no. 5,858,964 and Table 3, 5/7 (71.4%) of experimental mice survived more than 140 days after transplant as compared to 0/7 of PBS-treated control mice.

Please replace the paragraph beginning at page 39, line 3, with the following amended paragraph:

To test the effect of Copolymer 1 treatment on skin graft rejection in the B10.D2 → BALB/c model, BALB/c recipient mice were transplanted with skin grafts from B10.D2 donors and treated daily with: PBS ip from day -7, Copolymer 1 (ip + sc) from day -7. Grafts were inspected daily. Rejection was considered positive when no viable donor epidermis remained. The results are summarized in ~~Fig. 6 and in~~ Tables 4 and 6. The mean graft survival time (MST) in Copolymer 1-treated mice (600 μg/day) was 34 days in comparison to 26 days in PBS-treated mice (Table 6). In another experiment, treatment with 300 μg/day Copolymer 1 resulted in MST of 20.4 days and treatment with 600 μg/day resulted in 20.6 days, while the PBS control treatment resulted in MST of 16.1 days (Table 4). Thus Cop 1 induced significant beneficial effect on skin graft survival in the B10D2 → BALB/c system.

Please replace the paragraph beginning at page 39, line 35, with the following amended paragraph:

The results of thyroid transplantation are summarized in ~~Figs. 7 and 8 and in~~ Tables 5 and 7. The MFI of the Copolymer 1-treated mice (600 μg/day) was 3.2 folds in one experiment and 5.2 folds in another experiment over PBS-treated mice. Thus Copolymer 1 treatment was significantly effective in preventing the functional deterioration of transplanted thyroid grafts in the B10D2→BALB/c system.

Please replace the paragraph beginning at page 42, line 3, with the following amended paragraph:

As shown in ~~Fig. 7 and in~~ Tables 6 and 7, Copolymer 1 inhibited graft rejection in all strain combinations as demonstrated by the prolongation of the skin graft survival (Table 6) as well as by the elevation in the thyroid iodine absorbance (~~Fig. 7,~~ Table 7) in the Copolymer 1-treated mice in comparison to the PBS-treated mice. Copolymer 1 significantly inhibited even the rejection of grafts from donors of different H-2 haplotypes (Tables 4 and 6) which usually induce a more potent rejection course than the rejection of H-2 matched transplants. These results indicate that Copolymer 1 is effective in suppressing immune rejection of grafts from various origins in different strain

combinations, and thus may be effective in other species as well.

Please replace the paragraph beginning at page 44, line 2, with the following amended paragraph:

BALB/c recipient mice were transplanted with skin grafts originated in B10.D2 donors and treated daily with: PBS ip from day -7, Cop 1 (ip + sc) from day -7, CyA ip from day -7, and FK 506 ip 7 injections from day -2 before transplantation. Grafts were inspected daily. Rejection was considered positive when no viable donor epidermis remained. Thyroid glands from B10.D2 donors were transplanted in the kidney's capsules of BALB/c mice. The results are shown in ~~Figs. 6 and 8, and in~~ Tables 4 and 5. While CyA induced no significant beneficial effect in these systems, FK 506 significantly improved grafts survival/function in both the skin and the thyroid transplantation systems. Cop 1 also induced significant beneficial effect on graft survival/function similar to the effect of FK 506. While Cop 1 effect on skin graft survival was somewhat smaller than the effect of FK 506 (MST 20.6 for Cop 1 in comparison to 21.2 for FK 506 (Table 4 ~~and Fig. 6~~), Cop 1 was as effective as FK 506, in preventing the functional deterioration of transplanted thyroid grafts (3.2 and 3.1 folds over the PBS control for Cop 1 and FK 506 respectively, Table 5~~ and Fig. 8~~).